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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,904	11/24/2003	George Sgouros	D6348CIP	5297

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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
08/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/720,904	SGOUROS ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-59* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 34-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 November 2003 and 10 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the restriction in the reply filed on 6/15/07 is acknowledged. The traversal is on the ground(s) that the method of group III, claims 34-42 involve encapsulation of a radionuclide with an immunoliposome coated with molecules that enable targeting of the liposome to specific cells to reduce the loss of radioactive decay intermediates from the targeting vehicle and at the same time reduce non-tumor specific uptake of the radionuclide containing liposome. This is not found persuasive because the liposomes of group II, claims 20-33 contain a beta particle emitting radionuclide entrapped within the liposome which is not found in the invention of group III, claims 34-42. The liposomes of group II are different than liposomes of group III, would require a different search and thus pose a serious burden of search on the examiner. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 34-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group III, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 6/15/07.

3. Claims 1-19 and 43-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected groups I and IV, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/15/07.

Priority

Claims 20-33 are granted benefit of the priority date 12/16/02 of the parent document 10/319,978. Support for the recitation, "entrapping said radionuclide within small liposomal vesicles; incorporating said entrapped radionuclide into the aqueous phase of large lipsomes" of the instant claims 20-33 was not found in the provisional 60/212,186.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 20-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larsen et al. (US 6,592,843) in view of Scheinberg et al. (6,683,162B2) and Wartchow et al. (US2003/0082103A1)

6. Larsen et al. (US 6,592,843) discloses the encapsulation of radionuclides that emit alpha particles, such as ^{212}Pb, ^{225}Ac into a liposome to generate a radionuclide-liposome conjugator system with PEG affinic groups (column 2, lines 39-45, 57 and 59; column 3, lines 7-8). The PEG grafted liposomes have reduced interference from plasma proteins, and thus reduced the recognition and clearance affected by the macrophases of the reticuloendothelial system. Increased levels of tumor uptake due to sustained blood concentrations are thereby achieved (column 1, lines 45-50). The liposomes are of the typical size of 100nm (column 3, line 13). The radionuclide is

incorporated into the liposomal vesicle as a chelation compound where it is chelated to EDTA, DTPA, etc (column 3, lines 43-46). The PEG grafted liposomes of the disclosure can be further conjugated to folate labeled antibodies to target tumors and are stabilized in a PBS solution (phosphate containing buffer) (column 6, lines 1-18). The method of targeting cells in an individual involves administering the radionuclide-liposome conjugates to humans (column 6, lines 35-36). Larsen et al. does not disclose the antibodies to be herceptin, entrapping the radionuclide in a small liposome which is then incorporated into a large liposome or of liposomes having a diameter of about 600 to about 1000 nm.

7. Scheinberg et al. (6,683,162B2) discloses an ^{225}Ac complex attached to an antibody or fragment thereof, such as Herceptin and administered in doses from about 500 mCi to treat cancerous cells (column 2, lines 52-53; column 3, line 45; column 6, lines 6-11; column 18, table 4). The actinium-225 attached to a monoclonal antibody is delivered and internalized into a cell with enhanced potency and kills disseminated cancer cells (column 2, lines 24-31). The conjugate and a pharmaceutically acceptable carrier may be administered to humans to treat breast cancer (column 18, lines 16-17).

8. Wartchow et al. (US2003/0082103A1) discloses radiotherapeutic liposomal constructs comprising a radionuclide-chelator (DOTA) conjugation compound, targeting entity (antibody) and stabilizing entity (PEG) (p1, [0002]; p7, [0054]; p8, [0055 and 0057]; p10, [0077]). The radiotherapeutic liposomal constructs are used for the method of targeting cancerous tissue with radionuclides upon administration to a subject while leaving healthy tissue unaffected (p1, [0003]; p13, [0101]). The liposomes of the

disclosure may be bilayer structures that may have the therapeutic agent encapsulated (p9, [0075]) and be of the size 1000 nm (p10, [0078]). These multilamellar vesicles (MUV) are rapidly taken up into the reticuloendothelial system (the liver and spleen) which causes them to remain in the circulatory system for hours (p10, [0079]). The targeting agents may include herceptin, biotin, etc. (p12, [0099]; p14, [0105])

9. At the time of the invention it would have been obvious to one ordinarily skilled in the art to prepare radiotherapeutic liposomal constructs of the sizes 100 to 1000 nm where optimization of the size depends on the desired application, for instance uptake into the reticuloendothelial system. Warthchow et al. discloses that the radiotherapeutic liposomal constructs may be encapsulated within the MUV. One would have a reasonable expectation of success for attaching a targeting agent, such as herceptin or biotin to the liposome for site specificity.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
July 24, 2007

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER